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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/075,715	02/13/2002	Michael Chopp	1059.00073	9739

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EXAMINER	
GEMBEH, SHIRLEY V	
ART UNIT	PAPER NUMBER
1614	

MAIL DATE	DELIVERY MODE
10/04/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/075,715	CHOPP ET AL.	
	Examiner	Art Unit	
	Shirley V. Gembeh	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 July 2007* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 6-8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 6-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Status of Action

The response filed **7/17/07** presents remarks and arguments to the office action mailed **1/26/07**. Applicant's request for reconsideration of the rejection of claims in the last office action has been considered.

Applicant's arguments have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Status of claims

Claims 1, 6-8 are pending in this application.

Claims 2-5 and 9-13 are cancelled.

Claims 1 and 6-8 are amended.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 6-8 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Applicant has not provided a description of the structures of a representative number of compounds, nor a description of the chemical and/or physical characteristics of a representative number of compounds, nor a description of how to obtain a representative number of specific compounds.

In other words, the Applicant has not described with sufficient clarity what statins and phophodiesterase inhibitors are contemplated. The claims encompass any statin or phosphodiesterase known and unknown. A cursory examination of statins, for example, in related publications within the scientific literature indicates the existence of a very wide array of compounds. No distinguishing features by members of those broad genera have been provided in the instant disclosure. The scope of the claims extends to numerous structural variants, and the genera are highly variable. A significant number of structural differences among members of the genera are permitted. Structural features that augument efficacy in the claimed methods are missing from the disclosure.

No response to this rejection is noted.

Maintained Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 1 remains rejected under 35 U.S.C. 103(a) as being unpatentable over Cooke et al. US 5,428,070.

Cooke et al. teach administering L-arginine (see col. 3, lines 54-57) after vascular injury with emphasis on decreasing the effects of atherogenesis. Please note that atherosclerotic vascular diseases such as stroke is higher in patients with non–insulin-dependent diabetes mellitus, wherein the conditions may result in stroke. See col. 1, lines 33-48. The drug L-arginine is administered after the injury (post). See col. 3, lines 52-55 and cGMP is increased (see col. 9, lines 22-24) resulting in new neuron growth.

One of ordinary skill in the art would have been motivated to administer L-arginine to patients post stroke in order to promote neurogenesis, or growth of new neurons, because *L*-arginine is the substrate for nitric oxide (NO) production and has been shown to induce an endothelium-dependent increase in cerebral blood flow in humans.

Claims 1 and 6-8 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Cooke et al., US 5,428,070 taken with Liao, US 6,423,751, in view of Kaposzta, (*Circulation*. 2001;103:2371-2375), taken with Ohtsuka et al., The American J. of Med. Vol. 108, (5) 2000, 439.

Cooke is applied as above.

Liao teaches up-regulation of endothelial cell nitric oxide synthase expression (col. 3, lines 24-31) by administration of atorvastatin (col. 15, line 38). Liao teaches a surprising connection was made in the treatment of ischemic stroke wherein brain injury reduction is measured by determining a reduction in the infarct size in the treated versus the control groups. See col. 8, lines 59-65.

Kaposta teaches the administration of L-arginine in combination with S-nitroglutathione in the treatment of postoperative stroke risk. See page, 2371 background section.

Ohtsuka et al. teach cognitive functions increased with the administration of L-arginine (see report).

Combining the cited references would have been obvious to one of ordinary skill in the art to treat post-stroke patients. By administering L-arginine, cGMP is

increased. One of ordinary skill in the art would have been motivated to combine the prior art references and administer L-arginine topost-stroke patients in order to increase neurological function, such as cognition, because the references teach or suggest so. There are only two ways growth can occur: by either producing new neurons to replace the old or regeneration of old neurons, which is within the knowledge of one of ordinary skill in the art.

MPEP 2112.01"Products of identical chemical composition can not have mutually exclusive properties." A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). "Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not."

Nothing unobvious is seen in combining said cited art as they teach administering the same compounds (L-arginine, Statins) for the same type of disease (treating post-stroke).

The claimed invention was prima facie obvious to make and use at the time it was made.

Applicant argues that there is no disclosure for the regeneration of neurons, as is disclosed in the presently pending independent claims. Cooke et al. disclose the prophylactic use of L-arginine to maintain an enhanced level of nitric oxide in the vessel wall (col. 3, line 65 - col. 4, line 3), or, where atherosclerosis is "suspected", administration can begin at any time (col. 4, lines 55-57). There is no indication that this administration can be after an ischemic event and, further, there is further no evidence of an essential step of the presently pending claims of augmenting new neural growth or increasing neurological function.

Careful reconsideration of Applicants' argument has been given, but found unpersuasive. Liao teaches a surprising connection was made in the treatment of ischemic stroke wherein brain injury reduction is measured by determining a reduction in the infarct size in the treated versus the control groups. See col. 8, lines 59-65)

In view of the combined prior art, it would have been obvious to one of ordinary skill in the art to administer L-arginine for a post ischemic event. L-arginine is known for its properties of promoting neurogenesis (see Moskowitz, of record) and is also taught to increase cGMP levels (see above). Therefore, one of ordinary skill in the art would have been motivated to use and treat patients with post-ischemic stroke and expect success in doing so. In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a).

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Maintained Double Patenting (No arguments to this rejection are noted)

Claim **1, 6 - 12** are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims **1 - 13** of U.S. Patent Application No. **10,500,694**. Although the conflicting claims are not identical, they are not patentably distinct from each other. The reasons are as follows:

> Both sets of claims refer to treating neurological functions resulting from stroke, in the current application (claims 1,6-12), and neurological functions in general (claims 1 -13) in the copending application. The current application claims are an obvious variation of the copending application claims
>
> Both applications recite using the same compositions and/or derivatives thereof. See current application claims 1 and 6-12, wherein the compounds are selected from L-arginine, sildenafil, statins and phosphodiesterase inhibitors, and in the copending application claims 1-13, the compound is selected from phosphodiesterase inhibitors. The compositions recited in the claims are obvious of each other.

In view of the foregoing, the copending application claims and the current application claims are obvious variations.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shirley V. Gembeh whose telephone number is 571-272-8504. The examiner can normally be reached on 8:30 -5:00, Monday- Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SVG
9/17/07

Phyllis Spivack

PHYLLIS SPIVACK
PRIMARY EXAMINER